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=> s (anti pro-HB-EGF) and antibody
      504062 ANTI
          11 ANTIS
      504069 ANTI
                (ANTI OR ANTIS)
       91060 PRO
        1541 PROS
       92570 PRO
                (PRO OR PROS)
       84457 HB
        9694 HBS
       87354 HB
                (HB OR HBS)
       29309 EGF
          49 EGFS
       29320 EGF
                (EGF OR EGFS)
           0 ANTI PRO-HB-EGF
                (ANTI(W)PRO(W)HB(W)EGF)
      332216 ANTIBODY
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398187 ANTIBODIES
527656 ANTIBODY
(ANTIBODY OR ANTIBODIES)
L1 0 (ANTI PRO-HB-EGF) AND ANTIBODY

=> s (pro-HB-EGF) and antibody
91060 PRO
1541 PROS
92570 PRO
(PRO OR PROS)
84457 HB
9694 HBS
87354 HB
(HB OR HBS)
29309 EGF
49 EGFS
29320 EGF
(EGF OR EGFS)
30 PRO-HB-EGF
(PRO(W)HB(W)EGF)
332216 ANTIBODY
398187 ANTIBODIES
527656 ANTIBODY
(ANTIBODY OR ANTIBODIES)
L2 6 (PRO-HB-EGF) AND ANTIBODY

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L3 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:920630 CAPLUS
DN 147:421898
TI G protein .beta..gamma. subunits augment UVB-induced apoptosis by stimulating the release of soluble heparin-binding epidermal growth factor from human keratinocytes
AU Seo, MiRan; Lee, Mi-Jeong; Heo, Jin Hee; Lee, Yun-Il; Kim, Yeni; Kim, So-Young; Lee, Eun-So; Juhnn, Yong-Sung
CS Department of Biochemistry and Molecular Biology and Cancer Research Institute, Seoul National University College of Medicine, Seoul, 110-779, S. Korea
SO Journal of Biological Chemistry (2007), 282(34), 24720-24730
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology

DT Journal
LA English
AB UV radiation induces various cellular responses by regulating the activity of many UV-responsive enzymes, including MAPKs. The .beta..gamma. subunit of the heterotrimeric GTP-binding protein (G.beta..gamma.) was found to mediate UV-induced p38 activation via epidermal growth factor receptor (EGFR). However, it is not known how G.beta..gamma. mediates the UVB-induced activation of EGFR, and thus we undertook this study to elucidate the mechanism. Treatment of HaCaT-immortalized human keratinocytes with conditioned medium obtained from UVB-irradiated cells induced the phosphorylations of EGFR, p38, and ERK but not that of JNK. Blockade of heparin-binding EGF-like growth factor (HB-EGF) by neutralizing antibody or CRM197 toxin inhibited the UVB-induced activations of EGFR, p38, and ERK in normal human epidermal keratinocytes and in HaCaT cells. Treatment with HB-EGF also activated EGFR, p38, and ERK. UVB radiation stimulated the processing of pro-HB -EGF and increased the secretion of sol. HB-EGF in medium, which was quantified by immunoblotting and protein staining. In addn., treatment with CRM179 toxin blocked UV-induced apoptosis, but HB-EGF augmented this apoptosis. Moreover, UVB-induced apoptosis was reduced by inhibiting EGFR or p38. The overexpression of G.beta.1.gamma.2 increased EGFR-activating activity and sol. HB-EGF content in conditioned medium, but the sequestration of G.beta..gamma. by the carboxyl terminus of G protein-coupled receptor kinase 2 (GRK2ct) produced the opposite effect. The activation of Src increased UVB-induced, G.beta..gamma.-mediated HB-EGF secretion, but the inhibition of Src blocked that. Overexpression of G.beta..gamma. increased UVB-induced apoptosis, and the overexpression of GRK2ct decreased this apoptosis. We conclude that G.beta..gamma. mediates UVB-induced human keratinocyte apoptosis by augmenting the ectodomain shedding of HB-EGF, which sequentially activates EGFR and p38.
RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:217652 CAPLUS
DN 146:399418
TI Matrix metalloproteinase-7-catalyzed release of HB-EGF mediates deoxycholyltaurine-induced proliferation of a human colon cancer cell line
AU Cheng, Kunrong; Xie, Guofeng; Raufman, Jean-Pierre
CS Division of Gastroenterology and Hepatology, VA Maryland Health Care System and Program in Oncology, Greenebaum Cancer Center, University of Maryland School of Medicine, Baltimore, MD, 21201, USA
SO Biochemical Pharmacology (2007), 73(7), 1001-1012
CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier B.V.

DT Journal
LA English
AB Prior evidence indicates that bile acids stimulate colon cancer cell proliferation by muscarinic receptor-induced transactivation of epidermal growth factor receptors (EGFR). To explore further the mechanism underlying this action, we tested the hypothesis that bile acids activate a matrix metalloproteinase (MMP) that catalyzes release of an EGFR ligand. Initial studies showed that non-selective MMP inhibitors blocked the actions of deoxycholyltaurine (DCT), thereby indicating a role for MMP-catalyzed release of an EGFR ligand. DCT-induced cell proliferation was reduced by increasing concns. of EGFR kinase inhibitors, by antibodies to the ligand binding domain of EGFR, by neutralizing antibodies to heparin binding-EGF-like growth factor (HB-EGF) and by CRM197, an inhibitor of HB-EGF release. These findings and our observations with more selective MMP inhibitors suggested that MMP-7, an enzyme known to release HB-EGF, plays a key role in mediating bile acid-induced H508 colon cancer cell proliferation. We obsd. that recombinant HB-EGF and MMP-7 mimicked both the signaling and proliferative actions of bile acids. Strikingly, reducing MMP-7 expression with either neutralizing antibody or small interfering RNA attenuated the actions of DCT. MMP-7 expression in H508 cells was confirmed using quant. reverse transcription PCR. DCT stimulated a greater than 10-fold increase in MMP-7 gene transcription. Co-localization of pro-MMP-7 and pro -HB-EGF at the cell surface (immunofluorescence microscopy) was demonstrated, indicating proximity of the enzyme to its substrate. These findings provide strong evidence that in H508 human colon cancer cells, DCT-induced transactivation of EGFR is mediated by MMP-7-catalyzed release of the EGFR ligand HB-EGF.
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:925223 CAPLUS
DN 142:1315
TI Transactivation of epidermal growth factor receptor mediates catecholamine-induced growth of vascular smooth muscle
AU Zhang, Hua; Chalothorn, Dan; Jackson, Leslie F.; Lee, David C.; Faber, James E.
CS Departments of Cell and Molecular Physiology, School of Medicine, University of North Carolina, Chapel Hill, NC, USA
SO Circulation Research (2004), 95(10), 989-997
CODEN: CIRUAL; ISSN: 0009-7330
PB Lippincott Williams & Wilkins
DT Journal
LA English

AB Stimulation of .alpha.1-adrenoceptors induces proliferation of vascular smooth muscle cells (SMCs) and contributes to arterial remodeling. Although activation of NAD(P)H oxidase and generation of reactive oxygen species (ROS) are required, little is known about this pathway. In this study, the authors examd. the hypothesis that epidermal growth factor receptor (EGFR) transactivation and extracellular regulated kinases (ERK) are involved in .alpha.1-adrenoceptor-mediated SMC growth. Phenylephrine increased protein synthesis in assocn. with a rapid (.ltoreq.5 min) and sustained (.gtoreq.60 min) doubling of phosphorylation of EGFR and ERK1/2, but not p38 or JNK in the media of rat aorta maintained in organ culture. Antagonists of EGFR phosphotyrosine activity (AG-1478) and ERK phosphorylation (PD-98059, U-0126) abolished phenylephrine-induced protein synthesis, whereas antagonists of p38 or JNK phosphorylation had no specific effect. A competitive antagonist (P22) for heparin binding EGF-like growth factor (HB-EGF) blocked phenylephrine-induced protein synthesis, as did downregulation of pro-HB-EGF (CRM197). Phenylephrine-induced protein synthesis was inhibited by neutralizing antibody to HB-EGF and absent in HB-EGF-/- SMCs. Inhibitors of metalloproteinases (BiPS, KB-R7785) also blocked adrenergic growth. The neutralizing antibody against HB-EGF had no effect on the two-fold increase in ROS generation induced by phenylephrine (DCF fluorescence), suggesting that stimulation of NAD(P)H oxidase by .alpha.1-adrenoceptor occupation precedes HB-EGF release. Cell culture studies confirmed and extended these findings. These data suggest that .alpha.1-adrenoceptor-mediated SMC growth requires ROS-dependent shedding of HB-EGF, transactivation of EGFR, and activation of the MEK1/2-dependent MAP kinase pathway. This trophic pathway may link sympathetic activity to arterial wall growth in adaptive remodeling and hypertrophic disease.

RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:389324 CAPLUS

DN 139:115428

TI TACE cleavage of proamphiregulin regulates GPCR-induced proliferation and motility of cancer cells

AU Gschwind, Andreas; Hart, Stefan; Fischer, Oliver M.; Ullrich, Axel

CS Department of Molecular Biology, Max-Planck Institute of Biochemistry, Martinsried, D-82152, Germany

SO EMBO Journal (2003), 22(10), 2411-2421
CODEN: EMJODG; ISSN: 0261-4189

PB Oxford University Press

DT Journal

LA English

AB Communication between G protein-coupled receptor (GPCR) and epidermal

growth factor receptor (EGFR) signaling systems involves cell surface proteolysis of EGF-like precursors. The underlying mechanisms of EGFR signal transactivation pathways, however, are largely unknown. We demonstrate that in squamous cell carcinoma cells, stimulation with the GPCR agonists LPA or carbachol specifically results in metalloprotease cleavage and release of amphiregulin (AR). Moreover, AR gene silencing by siRNA or inhibition of AR biol. activity by neutralizing antibodies and heparin prevents GPCR-induced EGFR tyrosine phosphorylation, downstream mitogenic signaling events, cell proliferation, migration and activation of the survival mediator Akt/PKB. Therefore, despite some functional redundancy among EGF family ligands, the present study reveals a distinct and essential role for AR in GPCR-triggered cellular responses. Furthermore, we present evidence that blockade of the metalloprotease-disintegrin tumor necrosis factor-.alpha.-converting enzyme (TACE) by the tissue inhibitor of metalloprotease-3, a dominant-neg. TACE mutant or RNA interference suppresses GPCR-stimulated AR release, EGFR activation and downstream events. Thus, TACE can function as an effector of GPCR-mediated signaling and represents a key element of the cellular receptor cross-talk network.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:84701 CAPLUS

DN 134:126503

TI Angiotensin AT1 and AT2 receptors differentially regulate angiopoietin-2 and vascular endothelial growth factor expression and angiogenesis by modulating heparin binding-epidermal growth factor (EGF)-mediated EGF receptor transactivation

AU Fujiyama, Soichiro; Matsubara, Hiroaki; Nozawa, Yoshihisa; Maruyama, Katsuya; Mori, Yasukiyo; Tsutsumi, Yoshiaki; Masaki, Hiroya; Uchiyama, Yoko; Koyama, Yoko; Nose, Atsuko; Iba, Osamu; Tateishi, Eriko; Ogata, Nahoko; Jyo, Nobuo; Higashiyama, Shigeki; Iwasaka, Toshiji

CS Dep. Medicine II and Ophthalmology, Kansai Medical Univ., Oska, Japan

SO Circulation Research (2001), 88(1), 22-29
CODEN: CIRUAL; ISSN: 0009-7330

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB Angiotensin II (Ang II)-mediated signals are transmitted via heparin binding epidermal growth factor (EGF)-like growth factor (HB-EGF) release followed by transactivation of EGF receptor (EGFR). Although Ang II and HB-EGF induce angiogenesis, their link to the angiopoietin (Ang)-Tie2 system remains undefined. We tested the effects of Ang II on Ang1, Ang2, or Tie2 expression in cardiac microvascular endothelial cells expressing

the Ang II receptors AT1 and AT2. Ang II significantly induced Ang2 mRNA accumulations without affecting Ang1 or Tie2 expression, which was inhibited by protein kinase C inhibitors and by intracellular Ca2+ chelating agents. Ang II transactivated EGFR via AT1 and inhibition of EGFR abolished the induction of Ang2. Ang II caused processing of pro-HB-EGF in a metalloproteinase-dependent manner to stimulate maturation and release of HB-EGF. Neutralizing anti-HB-EGF antibody blocked EGFR phosphorylation by Ang II. Ang II also upregulated vascular endothelial growth factor (VEGF) expression in an HB-EGF/EGFR-dependent manner. AT2 inhibited AT1-mediated Ang2 expression and phosphorylation of EGFR. In an in vivo corneal assay, AT1 induced angiogenesis in an HB-EGF-dependent manner and enhanced the angiogenic activity of VEGF. Although neither Ang2 nor Ang1 alone induced angiogenesis, sol. Tie2-Fc that binds to angiopoietins attenuated AT1-mediated angiogenesis. These findings suggested that (1) Ang II induces Ang2 and VEGF expression without affecting Ang1 or Tie2 and (2) AT, stimulates processing of pro-HB-EGF by metalloproteinases, and the released HB-EGF transactivates EGFR to induce angiogenesis via the combined effect of Ang2 and VEGF, whereas AT2 attenuates them by blocking EGFR phosphorylation. Thus, Ang II is involved in the VEGF-Ang-Tie2 system via HB-EGF-mediated EGFR transactivation, and this link should be considerable in pathol. conditions in which collateral blood flow is required.

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L3 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2000:522173 CAPLUS

DN 133:217484

TI Heparin blockade of thrombin-induced smooth muscle cell migration involves inhibition of epidermal growth factor (EGF) receptor transactivation by heparin-binding EGF-like growth factor

AU Kalmes, Andreas; Vesti, Beatrice R.; Daum, Gunter; Abraham, Judith A.; Clowes, Alexander W.

CS Department of Surgery, University of Washington (Seattle), Sunnyvale, CA, USA

SO Circulation Research (2000), 87(2), 92-98
CODEN: CIRUAL; ISSN: 0009-7330

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB Agonists of G protein-coupled receptors, such as thrombin, act in part by transactivating the epidermal growth factor (EGF) receptor (EGFR). Although at first a ligand-independent mechanism for EGFR transactivation was postulated, it has recently been shown that this transactivation by

various G protein-coupled receptor agonists can involve heparin-binding EGF-like growth factor (HB-EGF). Because thrombin stimulation of vascular smooth muscle cell migration is blocked by heparin and because heparin can displace HB-EGF, we investigated the possibility that thrombin stimulation of smooth muscle cells (SMCs) depends on EGFR activation by HB-EGF. In rat SMCs, EGFR phosphorylation and extracellular signal-regulated kinase (ERK) activation in response to thrombin are inhibited not only by the EGFR inhibitor AG1478 and by EGFR blocking antibody but also by heparin and by neutralizing HB-EGF antibody. HB-EGF-dependent signaling induced by thrombin is inhibited by batimastat, which suggests a requirement for pro-HB-EGF shedding by a metalloproteinase. We further demonstrate that this novel pathway is required for the migration of rat and baboon SMCs in response to thrombin. We conclude from these data that the inhibitory effect of heparin on SMC migration induced by thrombin relies, at least in part, on a blockade of HB-EGF-mediated EGFR transactivation.
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT